

## **Opus 27 grant proposal: Innovative Small Molecule Inhibitors Targeting LAG-3 and MHCII Complex for Tumour Immunotherapy by dr Jacek Plewka**

My goal is to develop new, cost-effective treatments for cancer by creating small molecule inhibitors (SMIs) that can disrupt a LAG-3 protein interaction involved in the immune system's response to cancer.

Recent advancements in cancer treatment have shown that targeting specific proteins, like LAG-3, can greatly enhance the effectiveness of cancer immunotherapies. Currently, treatments that combine antibodies against PD-1 and LAG-3 have been approved by the FDA and have shown significant success. However, these treatments are extremely expensive, costing up to \$400,000 per quality-adjusted life-year.

My research aims to find more affordable alternatives by developing SMIs that can block the interaction between the LAG-3 protein and another protein called MHCII. This interaction is crucial for the immune system's ability to fight cancer. I have already identified a potential SMI through computer-based screening and experimental testing, which showed promising results in early tests. Moreover, its production price is only a fraction of the costs of currently used antibodies.

In addition to SMIs, I am also exploring other types of inhibitors, including peptides (short chains of amino acids), aptamers (short RNA or DNA molecules that can bind to specific targets), and compounds derived from natural sources to increase my chances of finding an effective molecule targeting the LAG-3.

Cancer remains one of the leading causes of death worldwide, and while recent therapies have shown great promise, their high cost makes them inaccessible to many patients. By developing more affordable treatments, I hope to make life-saving cancer therapies available to a broader population. By integrating organic chemistry, structural biology, and translational medicine, this research has the potential to transform cancer treatment, providing more effective and affordable options for patients worldwide.